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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,526	06/16/2000	Richard M. Lawn	99.395-A	9969

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/595,526	Applicant(s) LAWN ET AL.	
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-24,33 and 77-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-24,33 and 77-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 4-24, 33 and new claims 77-86 are now at issue and are present for examination.

Applicants' amendments and arguments filed on 10-3-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Examiner draws the attention of the applicants to the list of claims filed on 10-3-03. Applicants erroneously indicate that claims 1-2, 25-32, 34-76 as withdrawn, i.e., meaning that claims are still present in the application but are not under consideration. Claims 1-2, 25-32, 34-76 were cancelled by the applicant in the paper filed on 12-30-02 and are no longer present in the application and are not to be indicated as being withdrawn. Applicants are requested to acknowledge the cancellation of the above claims clearly in response to this Office action.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 3-24 and 33 of this application. Claims 3-24 and 33 are drawn to an isolated polynucleotide selected from the group consisting of a polynucleotide comprising SEQ ID NO:1, a polynucleotide encoding a polypeptide comprising SEQ ID NO:2, a polynucleotide comprising nucleotides 291-7074 of SEQ ID NO:1 and a polynucleotide encoding a polypeptide having 98% identity to SEQ ID NO:2 and claims the benefit of domestic priority to provisional applications filed on 6-18-99, 9-14-99 and 11-19-99. However, none of the provisional application disclose the full length sequence of either SEQ ID NO:1 or 2. Instead

the provisional application 60/140,264 filed on 6-18-99 discloses the nucleotide sequence and the encoded amino acid sequence with accession No. AJ012376, published by Langmann et al. in 1999. Applicants do not disclose specifically either SEQ ID NO:1 or 2 and therefore Examiner has not granted the benefit of priority date.

In response to the previous Office action, applicants have not responded to the above. Examiner has not granted the benefit of priority date.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 77, 5-6 and claims 78-86, 7-24 which depend therefrom respectively are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 77 and 5-6 recite the phrase "polynucleotide having ABC1 activity" which leads one to conclude that the polynucleotide itself has the ABC1 activity. However, it is well known that polynucleotide sequences do not possess the property or activity of polypeptides. It appears that applicants intended to mean "polynucleotide encoding a polypeptide with ABC1 activity". If that is so amending the claim accordingly would overcome the above rejection. (Examiner has also not reinstated the rejection of above claims under 356 U.S.C. 112, Ist paragraph as lacking written description concluding that applicants intended to claim a polynucleotide encoding a polypeptide with ABC1 activity). Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 13, 16, 20, 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA comprising a polynucleotide with SEQ ID NO:1, does not reasonably provide enablement for any polynucleotide comprising a polynucleotide that is either 90% or 95% sequence identity with SEQ ID NO:1 or any vectors and host cells comprising such polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5-7, 13, 16, 20, 23 are so broad as to encompass any DNA which is 90% or 95% similar to SEQ ID NO:1, and vectors and host cells comprising such DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

Applicants propose to use the above polynucleotides for processes such as recombinant protein preparation. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent

homology (more than 99%) can be used for such purposes, changing the nucleotide sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:1 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that will result in transcribing of unrelated mRNAs and may not lead to the translation of the polypeptide of interest. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single ABC1 transporter protein.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding a ABC1 transport protein because the specification does not establish: (A) regions of the DNA sequence encoding ABC1 polypeptide which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of ABC1 encoding DNA sequences to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in the above polynucleotide with an expectation of obtaining the desired biological function and utility; and (D) the specification

provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA comprising a polynucleotide that is either 90% or 95% identical to SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection arguing at length and n summary that the specification provides enough teaching for the invention to be fully enabled. However, such arguments are still not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with detailed guidance (not a guidance of general nature) as to where to make the changes and for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the

direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the DNA sequence encoding ABC1 polypeptide which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of ABC1 encoding DNA sequences to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in the above polynucleotide with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Hence the above rejection is maintained for claims 5-7, 13, 16, 20, 23.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-24 and 33 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rosier-Montus et al. (US 20020146792A1, published on 10-10-02, with a priority date of 5-2-2000). Claims 3-24 and 33 are drawn to an isolated polynucleotide selected from the group consisting of a polynucleotide comprising SEQ ID NO:1, a polynucleotide encoding a polypeptide comprising SEQ ID NO:2, a polynucleotide comprising nucleotides 291-7074 of SEQ ID NO:1 and a polynucleotide encoding a polypeptide having 98% identity to SEQ ID NO:2, wherein the polynucleotide is complementary to the above polynucleotides, a polynucleotide that is at least 90% or 95% identical to the above polynucleotides, a composition of the above polynucleotides with a suitable carrier, a vector comprising the above polynucleotide, a recombinant vector comprising the above polynucleotide linked to a heterologous promoter such as cytomegalovirus (CMV) promoter, a composition comprising the recombinant vector and a host cell comprising the above vectors and a method of making the polypeptide comprising transfecting a mammalian host cell with a recombinant vector followed by culturing and purifying the expressed polypeptide. Rosier-Montus et al. disclose a polynucleotide (published as SEQ ID NO:10 by Rosier-Montus et al.) that encodes a polypeptide which is more than 98% identical to SEQ ID NO:2 (see previously provided sequence alignments). The reference also discloses complementary sequences, and composition with suitable carrier, vectors comprising the above polynucleotide linked to heterologous promoter and composition comprising the same. While the reference does not explicitly disclose the polynucleotide linked to a CMV promoter in a specific vector such as pCEPh or a host cell comprising the same or a method of producing the polypeptide by transfecting a mammalian host cell, such steps would have been obvious to one of ordinary skill

in the art. This is because, as the polynucleotide has been isolated from a mammalian cell which harbors extensive post translational machinery, it would have been obvious to one of ordinary skill in the art to make recombinant protein for studying its properties in further detail, in a mammalian host cell using commercially available vectors comprising CMV promoters such as pCEPh, such that the protein will be exposed to same type of post translational machinery for post translational processing of the protein. Therefore, claims 3-24 and 33 would have been either anticipated or in the alternative rendered *prima facie* obvious by Rosier-Montus et al. to one of ordinary skill in the art.

In response to the previous rejection, applicants have filed a 37 CFR 1.131 declaration signed by a single inventor. However, said declaration is found to be deficient for the following reasons. Hence the above rejection is maintained for reasons of record until such time that the above declaration is perfected.

The declaration filed on 9-25-03 under 37 CFR 1.131 has been considered but is ineffective to overcome the Rosier-Montes et al. The evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Rosier-Montes et al. reference. Applicants must clearly provide for in their declaration that the conception and reduction to practice and the establishment of a date of completion of their invention was conducted or performed in this country or in a NAFTA country or a WTO member country. See MPEP 715. Furthermore, the declaration must be signed by all inventors. Therefore, the above declaration has been found to be deficient.

Conclusion

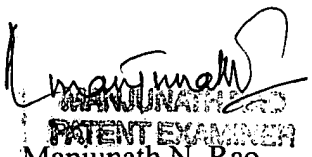
None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating

to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
December 22, 2003